

REMARKS**I. Status of the Claims**

Claim 1 is pending.

Claims 2-27 were previously withdrawn in response to a restriction requirement.

II. Claim 1 is Not Obvious Over Taylor-Papadimitriou *et al.*

On page 3 of the Office Action (“Action”), the examiner rejected claim 1 under § 103(a) as being unpatentable over Taylor-Papadimitriou *et al.*, in view of Hopp *et al.*

The examiner admits:

While Taylor-Papadimitriou *et al.* do not explicitly disclose the details of step (a)-(b) and (e)-(g)

but argues that the steps “are well-recognized skills in the art” referring, *e.g.* to Hopp (Action, page 4).

Step (a) of claim 1 states “obtaining amino acid sequence of an extracellular domain of a receptor or receptor-like molecule”. Neither Taylor-Papadimitriou *et al.* nor Hopp *et al.* mention or suggest to obtain a sequence of the extracellular domain of **a receptor or a receptor-like molecule**. Taylor-Papadimitriou merely mentions that not all mucins are transmembrane molecules (page 228, right column). In addition, some of the mucins are secreted molecules and are poorly retained on the cell surface (page 14, lines 8-10 of the specification). Therefore Taylor-Papadimitriou does not state or suggest obtaining an amino acid sequence of an extracellular domain of a receptor or receptor-like molecule.

Step (b) of claim 1 states “mapping hydrophilic regions of the domain by analyzing the amino acid sequence of the domain employing a rolling sum analysis of 7 consecutive residues”. Although rolling sum analysis is a known technique to analyze antigenic determinants, Taylor-Papadimitriou neither mentions nor suggests performing a rolling sum analysis on an extracellular

domain of a receptor or receptor like molecule. Hopp generally discusses prediction of hydrophilicity through a hexapeptide analysis and does not refer to a rolling sum analysis of seven consecutive amino acid residues in the extracellular domains of a receptor or receptor like molecule.

It is to be noted, however, that citing references which **merely indicate that isolated elements and/or features** recited in the claims are known **is not a sufficient basis** for concluding that the combination of claimed elements would have been obvious. *Ex parte Hiyamizu* (BPAI 1988) 10 PQ. 2d 1393 (*emphasis added*).

Step (d) of claim 1 states “locating amino acids that are susceptible to modification in the absence of steric hindrance by glycoside chains”. Neither Taylor-Papadimitriou nor Hopp teach or suggest performing a susceptibility determination of the flanking amino acids in the absence of steric hindrance by adjacent glycosidic chains. On page 25, lines 4-8, the present specification discloses that “the deglycosylated peptide regions are evaluated for the inclusive presence of amino acids that are susceptible to alteration in the absence of glycoside chains which normally would sterically restrict the contact of enzyme or other agents with the amino acids susceptible to molecular modification”. Taylor-Papadimitriou in view of Hopp does not teach or suggest performing a susceptibility determination as in step (d) of claim 1. “Obviousness requires **a suggestion of all limitations** in a claim”. *CFMT, Inc. v. Yieldup Int'l Corp.*, 2003 U.S. App. LEXIS 23072 (Fed. Cir. 2003) (*emphasis added*). Therefore, Taylor-Papadimitriou in view of Hopp does not render claim 1 obvious.

In addition, step (e) of claim 1 states “synthesizing candidate peptides that fit the criteria of steps (a) to (d)”. Neither Taylor-Papadimitriou nor Hopp teach or suggest synthesizing peptides that have certain desirable characteristics referred to in steps (a)-(d) of claim 1. Taylor-Papadimitriou describes glycosylation patterns in PEM, a product of the MUC1 gene and possible mABs directed against the entire protein. Taylor-Papadimitriou does not suggest synthesizing peptides as in claim 1. Nor does Taylor-Papadimitriou suggest “labeling the peptides at either end of

their amino acid sequence” as in step (f) of claim 1. Furthermore, step (g) of claim 1 states “testing whether the candidate peptides are cancer-specific or cancer associated”. On page 230, right column, Taylor-Papadimitriou *et al.*, state:

It should be noted, however, that the same mucin **may be glycosylated differently by different normal tissues**. [T]his degree of complexity means that analysis of mucin expression with **antibodies can be difficult to interpret**. (*emphasis added*).

Therefore, a mere knowledge of the role of glycosylation is not enough to motivate a person of ordinary skill in the art to practice the claimed method, which is to differentiate normal cells from cancer cells by synthesizing specific cancer-specific or cancer-associated peptide antigens.

In *Nursery Supplies*, the court held:

One cannot simply backtrack from the invention to find a connection to the prior art. Hindsight must be avoided. See *W.L. Gore and Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983). Rather, **one must start with the prior art and find some suggestion or motivation** either in a single reference to modify it to produce the claimed invention, [] or some suggestion or motivation in a group of references to combine them to produce the claimed invention. *Nursery Supplies v. Lerio Corp.*, 45 U.S.P.Q.2d (BNA) 1332 (M.D. Pa. Sept. 19, 1997). (*emphasis added*).

To properly combine two references to reach a conclusion of obviousness, there must be some teaching, suggestion or inference in either or both of the references, or knowledge generally available to one skilled in the art, which would have led one to combine the relevant teachings of the two references. *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc. et al.* (CAFC 1985) 776 F. 2d 281, 227 USPQ 657; *Ex parte Levengood, supra*. Both the suggestion to make the claimed composition or device or carry out the claimed process and the reasonable expectation of success must be founded in the prior art, not in applicant’s disclosure. *In re Vaeck* (CAFC 1991) 947 F. 2d 488, 20 PQ. 2d 1438. The references, viewed by themselves and not in retrospect, must suggest doing what applicant has done. *In re Shaffer* (CCPA 1956) 229 F. 2d 476, 108 USPQ 326; *In re Skoll* (CCPA 1975) 523 F. 2d 1392, 187 USPQ 481. The examiner has not demonstrated teachings

to combine Taylor-Papadimitriou *et al.* with teaching in the art.

Although Taylor-Papadimitriou describes the changes in glycosylation and expression of mucins with particular emphasis on polymorphic epithelial mucin (PEM), the product of the MUC1 gene in tumors and normal tissues, it fails to teach or suggest all the steps in claim 1. Hopp merely describes a standard technique to predict hydrophilicity. On pages 3-4 of the Action, the examiner quotes from Taylor-Papadimitriou:

It has been known for many years that the surface molecules of cancer cells can undergo changes in their glycosylation profile. In recent years, however, these changes have been defined in more detail and it is now possible to take a more directed approach to exploiting them in the diagnosis and treatment of cancer.

However, the above-mentioned paragraph is too vague to suggest or motivate a person of ordinary skill in the art to come up with a method that has all the steps mentioned in claim 1. Taylor-Papadimitriou merely alludes to a possibility that a "more directed approach" may be pursued to diagnose and treat cancer. Taylor-Papadimitriou does not suggest what that approach might be. It would be a major jump in logic from the statement in Taylor-Papadimitriou to come up with the steps (a)-(g) of claim 1.

The legal standard for a *prima facie* case of obviousness is **not** to show that all individual elements of a claim are known to those of skill in the art (which in any case the examiner has **not** proved) but to show a teaching or suggestion to combine the elements. The examiner fails to make the showing, therefore a *prima facie* case of obviousness is not established.

To establish *prima facie* obviousness of a claimed invention, **all the claim limitations must be taught or suggested by the prior art.** In *re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In *re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970) (*emphasis added*).

The sequence of steps (a)-(g), which is to practice the claimed method is neither taught nor suggested in Taylor-Papadimitriou or Hopp, or their combination.

A statement that modifications of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art at the time the claimed invention was made' " because the references relied upon teach that all aspects of the claimed invention were **individually known in the art is not sufficient to establish a prima facie case of obviousness** without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000) (emphasis added).

In the present action, the examiner merely states his opinion and does not offer evidentiary support how knowledge of the role of glycosylation will motivate a person of ordinary skill in the art to obtain hydrophilic sequence of the extracellular domain of a receptor or receptor-like molecule, performing rolling sum analysis, locating amino acids **that are susceptible to modification in the absence of steric hindrance by glycoside chains**, and **synthesizing those peptides** and testing by an *in vitro* assay that the peptides are cancer-specific or cancer associated as disclosed in claim 1. Therefore, even if Taylor-Papadimitriou *et al.*, and Hopp were combined, a person of ordinary skill in the art would not have come up with the claimed invention.

In summary, although some steps in claim 1 may represent known techniques, based on the foregoing analysis of facts and law, claim 1 considered in its entirety, represents a novel and non-obvious method over Taylor-Papadimitriou in view of Hopp. Applicants request withdrawal of the 103 (a) rejection.

III. Other issues

Applicant thanks the examiner for withdrawing the 112 rejection.

Applicants request allowance of the pending claim.

No other fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21417/91482).

Respectfully submitted,

BARNES & THORNBURG

A handwritten signature in cursive script, appearing to read "Alice O. Martin", written over a horizontal line.

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